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TI Molecular biology of blood-brain barrier ontogenesis and function.
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AB The vascular system of the central nervous system is derived from capillary endothelial cells, which have invaded the early embryonic neuroectoderm. This process is called angiogenesis and is probably regulated by brain-derived factors. Vascular endothelial cell growth factor (VEGF) is an angiogenic growth factor whose expression correlates with embryonic brain angiogenesis, i.e. expression is high in the embryonic brain when angiogenesis occurs and low in the adult brain when angiogenesis is shut off under normal physiological conditions. VEGF is also a vascular permeability factor (VPF) and, therefore, its expression is also consistent with the formation of the blood-brain barrier by brain endothelial cells, i.e. capillaries are leaky in the embryonic brain but are tight in the postnatal and adult brain. Thus, VEGF/VPF may be a key factor regulating endothelial cell growth and permeability. This notion is further supported by the observation that VEGF expression is induced and strongly upregulated in human malignant glioblastoma. This tumor is characterized by vascular proliferations, vascular leakage and edema. The differentiation of blood-brain barrier endothelial cells is probably regulated by astrocytes which form foot processes apposed to the abluminal vascular basement membrane. Blood-brain barrier endothelial cells express a set of cell surface proteins that are absent from permeable capillaries. We have characterized one such novel transmembrane glycoprotein which is a new member of the immunoglobulin superfamily. This protein and the analysis of the in vitro characteristics of brain endothelial cells may help to define the molecular mechanisms that are involved in blood-brain barrier induction and permeability.